Gynecologic Oncology Reports 1 (2011) 20–21

Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case Report

Severe ulceration over mandibular torus in an ovarian cancer patient receiving bevacizumab therapy

Deanna Teoh [a], John S. Won [b], Robert Eisberg [c], Kimberly Nolte [a], Angeles Alvarez Secord [a,*]

[a] Division of Gynecologic Oncology, Duke Comprehensive Cancer Center, Durham, NC 27710, USA
[b] Preston Oral-Maxillofacial Surgery, Cary, NC 27513, USA
[c] Atlantic Family Dental, Raleigh, NC 27604, USA

ARTICLE INFO

Article history:
Received 11 July 2011
Accepted 6 September 2011
Available online 14 September 2011

Keywords:
Ovarian cancer
Bevacizumab

A 64 year-old Caucasian female with advanced stage, poorly-differentiated ovarian cancer diagnosed five years earlier developed progressive disease while receiving carboplatin and paclitaxel for recurrent disease. Treatment was changed to docetaxel 40 mg/m^2 and bevacizumab 15 mg/kg 21 days, with intravenous dexamethasone 20 mg administered as part of the pre-chemotherapy medication regimen. The patient initially complained of jaw pain after three cycles of chemotherapy, which she attributed to temporomandibular joint disorder. The patient continued to have problems with jaw pain and mucositis, and after five cycles reported removal of a large piece of oral "plaque," with subsequent improvement of her symptoms. She was seen by an oral maxillofacial surgeon after losing another large piece of plaque. The differential diagnosis included osteonecrosis of the jaw which has been reported with bevacizumab (Guarneri et al., 2010). Oral exam revealed a small ulceration on the lingual surface of the left mandible at a site of exostosis, and a 1×1 mm defect with mucosal covering distal to the second molar. The severity of epithelial breakdown exceeded that seen in typical ulcers. Maxillofacial CT and plain films (Fig. 1) showed no evidence of metastatic disease or osteonecrosis. The patient was diagnosed with mucosal ulceration associated with torus mandibularis. She had not previously been diagnosed with torus mandibularis but this probably was a pre-existing condition. The symptoms resolved with oral hygiene, including a magic mouthwash solution containing nystatin 100,000 units/ml, hydrocortisone 60 mg and diphenhydramine HCL, and no further dental therapy was necessary. The chemotherapy and bevacizumab were held for one week providing a 4-week respite from therapy. She subsequently received three additional cycles of bevacizumab and docetaxel for a total of nine cycles, followed by two additional cycles of single-agent bevacizumab. She ultimately developed progressive disease, and chemotherapy was changed to her current regimen of liposomal doxorubicin.

Review of the literature

To our knowledge, this is the first report in the literature of mucosal ulceration over torus mandibularis in an ovarian cancer patient treated with bevacizumab. Torus mandibularis is a hyperplastic bone which presents as a bony mass on the lingual side of the mandible. Torus mandibularis and the related conditions torus palatines and buccal and palatal exostoses are thought to be multifactorial in etiology. The incidence of tori varies widely in the literature, from 1.4 to 69.7%, due to differences in study population ethnicities. In a study of 448 females in the metropolitan area of Washington, D.C. the prevalence of torus mandibularis was 38.7%, and slightly more common in Caucasians compared to African Americans, Hispanics, Asians or Native Americans (Chohayeb and Volpe, 2001). This study showed no association with age, but other studies have shown that tori occur more commonly in young and middle-aged adults (Jainkittivong and Langlais, 2000). Torus palatinus is more common in women, while torus mandibularis is more common in males (Jainkittivong and Langlais, 2000; Lo et al., 2011). The presence of tori may be positively correlated with bone mineral density (Lo et al., 2011). The most direct cause of tori formation is masticatory stress and bruxism (Jainkittivong and Langlais, 2000).

There are no reports regarding bevacizumab-associated dental ulceration over torus mandibularis. Bevacizumab is a humanized monoclonal antibody that binds to and inhibits VEGF. VEGF inhibition may cause avascularization and compromise of the mucosa or osteon, allowing greater trauma from everyday activities such as chewing and toothbrushing, and decreased ability to repair itself. Since tori protrude from the alveolar bone it's more exposed to mechanical abrasive situation where "weakened" mucosa would break down easily compared to healthy gingival tissue. Inhibition of VEGF, which plays a role in the upregulation of osteoclasts, could compromise the bone remodeling required to repair even minor trauma, and result in localized bone necrosis and periosteal death. Therefore, it is

* Corresponding author at: DUMC 3079, Gynecologic Oncology, Duke University Medical Center, Durham, NC 27710, USA. Fax: +1 919 684 8719.
E-mail address: secor002@mc.duke.edu (A.A. Secord).

doi:10.1016/j.gynor.2011.09.001

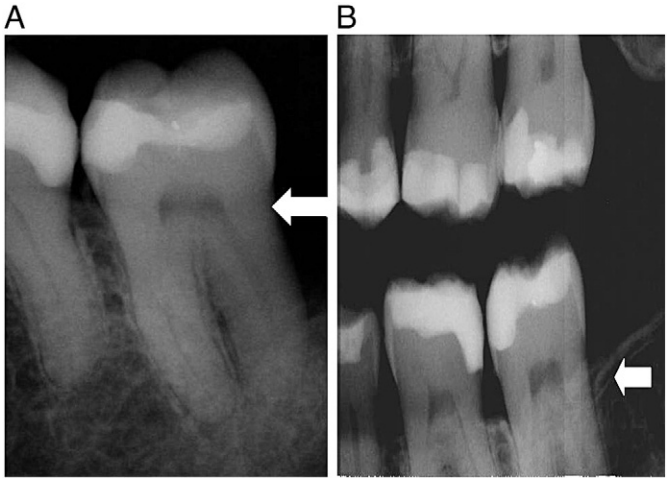

Fig. 1. A) Arrow shows radiograph of bone level two years prior to reported tissue loss; B) Arrow shows bone level at the time of presentation, indicating significant bone loss.

possible that if the bevacizumab had not been held that the ulceration may have progressed to osteonecrosis of the jaw.

While our patient was not taking bisphosphonates many women do receive this therapy. Thus it is important to note that in a review of 923 women taking bisphosphonates, 28% were found to have oral tori, exostoses, or both (Lo et al., 2011). In contrast to population-based studies showing a higher prevalence of tori palatinus in females, this study showed a slightly higher incidence of lingual mandibular tori (15.8% vs. 13.9%). Of the 128 patients with a diagnosis of tori palatinus, two (1.6%) eventually developed bisphosphonate-related osteonecrosis of the jaw. The association between bisphosphonates and oral tori/exostoses is unclear. However, the bony protrusions cause the overlying tissue to become stretched and atrophic, predisposing the area to trauma. Inhibition of osteoclasts by bisphosphonates may interfere with the bone remodeling necessary for wound-healing, and increase susceptibility to osteomyelitis and bone necrosis (Guarneri et al., 2010).

Although a cause-and-effect relationship cannot be established, it is important to recognize that these bony protuberances are areas which can be easily traumatized, and that bevacizumab or other anti-angiogenic agents may predispose patients to dental ulcerations which if unrecognized may degenerate to osteonecrosis of the jaw. In conclusion, this case report illustrates the potential for mucosal ulceration over a benign torus mandibularis in the setting of bevacizumab treatment and emphasizes the need for close monitoring of dental symptoms.

Conflict of interest statement

No conflict of interest.

References

Guarneri, V., Miles, D., Robert, N., Dieras, V., Glaspy, J., Smith, I., et al., 2010. Bevacizumab and osteonecrosis of the jaw: incidence and association with bisphosphonate therapy in three large prospective trials in advanced breast cancer. Breast Cancer Res. Treat. 122, 181–188.

Chohayeb, A.A., Volpe, A.R., 2001. Occurrence of torus palatines and mandibularis among women of different ethnic groups. Am. J. Dent. 14, 278–280.

Jainkittivong, A., Langlais, R.P., 2000. Buccal and palatal exostoses: prevalence and concurrence with tori. Oral Surg. Oral Med. Oral Pathol. 90, 48–53.

Lo, J.C., O'Ryan, F., Yang, J., Hararah, M.K., Gonzalez, J.R., Gordon, N., et al., 2011. Oral health considerations in older women receiving oral bisphosphonate therapy. J. Am. Geriatrics Soc. 59, 916–922.